

IN THE SPECIFICATION:

Please delete the section of the specification entitled "BRIEF DESCRIPTION OF DRAWINGS" starting on page 25 and ending of page 27 of the originally filed specification, and replace it with the following section:

BRIEF DESCRIPTION OF DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

FIG. 1: Schematic drawing of the pBr/Ad.Bam-rITR construct.

FIG. 2: Schematic drawing of the strategy used to delete the fiber gene from the pBr/Ad.Bam-rITR construct, using primers NY-UP (SEQ ID NO: 36) and NY-DOWN (SEQ ID NO: 37).

FIG. 3: Schematic drawing of construct pBr/Ad.BamRDfib.

FIG. 4: Nucleotide sequence of ~~chimaeric~~ chimeric fiber Ad5/16, SEQ ID NO: 32.

FIG. 5: Schematic drawing of the construct pClipsal-Luc.

FIG. 6: Schematic drawing of the method to generate chimaeric adenoviruses using three overlapping fragments. Early (E) and late regions (L) are indicated. L5 is the fiber coding sequence.

FIGS. 7A & 7B: Sequences including the gene encoding adenovirus 16 fiber protein as published in Genbank with nucleotide sequence SEQ ID NO: 33 and amino acid sequence SEQ ID NO: 35; and sequences including a gene encoding a fiber from an adenovirus 16 variant as isolated in the present invention with nucleotide sequence SEQ ID NO: 38 and amino acid sequence SEQ ID NO: 34, wherein the sequences of the fiber protein are from the NdeI-site. FIG. 7A nucleotide sequence comparisons of SEQ ID NO: 33 and SEQ ID NO: 38. FIG. 7B amino-acid comparisons of SEQ ID NO: 35 and SEQ ID NO: 34.

FIG. 8 : Infection of synoviocytes using different amounts of virus particles per cell (MOI) and two different adenoviruses: Ad5=Ad5.Clip.Luc; Ad5/16= Ad5.Luc-fib16. Luciferase transgene expression, 48 hours after a 2 hours infection procedure is depicted as relative light

units (=RLU) per microgram whole cell lysate. Error bars represent standard error of the mean (SEM).

FIG. 9: Infection of synoviocytes using different concentrations of cells. Luciferase transgene expression, 48 hours after a 2 hours infection procedure is depicted as relative light units (=RLU) per microgram total protein. Error bars represent SEM. The actual MOI differed between the cell concentrations and ranged from 20,000 virus particles per cell (cell density 12,500) to 2,500 virus particles per cell (cell density 100,000).

FIG. 10: Infection of synoviocytes using different virus exposure periods. Luciferase transgene expression, 48 hours after either a 2 hours or a 20 hours virus exposure is depicted as relative light units (=RLU) per microgram protein. Error bars represent standard deviations.

FIG. 11: Synoviocytes were incubated with IG.Ad.CMV.TK or IG.Ad.mlp-I.TK. Cells were cultured with or without GCV.

FIG. 12: Bystander killing was assessed in cultures containing both TK-infected and non-TK-infected synoviocytes in a proportion 0/100, 50/50, 25/75 and 0/100. Cells were cultured with or without GCV.

~~FIGs.~~ FIGS. 13 A & B: X-gal expression in synovial tissue 3 days after intra-articular injection of IG.Ad.CMV.lacZ in the knee. 13A: macroscopy. 13B: direct LacZ staining of synovial tissue counterstained with Mayers Hamalanlosung.

FIG. 14 is a graph comparing infection of Ad5.luc and Ad5.fib16.luc on RA synoviocytes.

FIG. 15 is a graph depicting the percentage of lacZ positive cells with Ad5.lacZ and Ad5.fib16.lacZ in RA synoviocytes.

FIG. 16 A & 16B are graphs depicting the infection efficiency of Ad5.GFP and Ad5.fib16.GFP in RA synoviocytes and the respective luciferase counts respectively.

FIG. 17 is a graph depicting the infectivity of chimeric adenoviruses on RA synoviocytes.

FIG. 18A is a graph depicting the percentage of infected cells with three B-type fiber-modified viruses on RA synoviocytes.